

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/B2005/000872

International filing date (day/month/year)
01.04.2005

Priority date (day/month/year)
13.04.2004

International Patent Classification (IPC) or both national classification and IPC
C07C255/54, C07C323/41, C07D317/58, C07D307/79, C07D285/14, C07D311/76, C07D209/16, C07D471/04,

Applicant
WARNER-LAMBERT COMPANY LLC

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Docketed

DATE 8/29/2005
FOR Response - IMD
BY: TRM CHECKED BY: _____

Name and mailing address of the ISA:



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Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
☐ a sequence listing
☐ table(s) related to the sequence listing
 - b. format of material:
☐ in written format
☐ in computer readable form
 - c. time of filing/furnishing:
☐ contained in the international application as filed.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43bis.1 and 64.1) is the claimed priority date.
2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,
☒ claims Nos. 1-15 (all in part)

because:

- ☒ the said international application, or the said claims Nos. 10 (with respect to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):

see separate sheet

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-15 (all in part) are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for the whole application or for said claims Nos.

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

- ☐ has not been furnished
☐ does not comply with the standard

the computer readable form

- ☐ has not been furnished
☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

- ☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2,4,7,10-15
	No: Claims	1,3,5,6,8,9
Inventive step (IS)	Yes: Claims	2,4,7,10-15
	No: Claims	1,3,5,6,8,9
Industrial applicability (IA)	Yes: Claims	1-9, 11-15
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

and /or

2. Non-written disclosures (Rules 43bis.1 and 70.9)

see form 210

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The scope of the present claims 1 - 15 in as far as the expression "prodrug" is concerned is so unclear that a meaningful International Search is impossible with regard to this expression. Consequently, a complete written opinion concerning the present application is limited to those parts of the claims for which a complete international search report was established (Rule 43bis.1(b) with reference to Rule 66.1(e) PCT).

It should in particular be understood that any positive statement as to novelty and/or inventive step exclusively relates to said limited subject-matter.

Claim 10 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Reference is made to the following documents:

- D1: WO 02/060896 A (PFIZER PRODUCTS INC; CHAMBERS, ROBERT, JAMES; MAGEE, THOMAS, VICTOR; M) 8 August 2002 (2002-08-08)
- D2: LOEFFLER L J ET AL: "SYNTHESIS OF ISOSTERES OF P-AMIDINOPHENYLPYRUVIC ACID INHIBITORS OF TRYPSIN, THROMBIN, AND PANCREATIC KALLIKREIN" 1 March 1975 (1975-03-01), JOURNAL OF MEDICINAL CHEMISTRY, AMERICAN CHEMICAL SOCIETY. WASHINGTON, US, PAGE(S) 287-292 , XP000574801 ISSN: 0022-2623
- D3: EP-A-0 002 309 (IMPERIAL CHEMICAL INDUSTRIES PLC) 13 June 1979 (1979-06-13)
- D4: WO 03/065992 A (GTX, INC; STEINER, MITCHELL, S; VEVERKA, KAREN, A; MILLER, DUANE, D; D) 14 August 2003 (2003-08-14)

1. Novelty

1.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1, 3, 5, 6, 8 and 9 is not new in the sense of Article 33(2) PCT.

The documents D1 - D3 (see D1 - D3, passages indicated in the International Search Report) describe already compounds falling within the scope of the present claims 1, 3, 5, 6, 8 and 9.

1.2 The subject-matter of claims 2, 4, 7 and 10 - 15 appears to be novel with regard to the available prior art.

2. Inventive Step

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1, 3, 5, 6, 8 and 9 does not involve an inventive step in the sense of Article 33(3) PCT. Since the subject-matter of claims 1, 3, 5, 6, 8 and 9 is not novel, it cannot be regarded as inventive either.

2.2 To the subject-matter of claims 2, 4, 7 and 10 - 15 the following applies:

Document D4, which discloses selective androgen modulators is regarded as representing the closest prior art. In view of D4 the problem underlying the present application can be defined as providing further selective androgen modulators. To solve this problem the applicant provides the compounds according to the present application, which differ from the compounds disclosed in D4 in the chain which is attached to the 4-position of the 1-cyano-2-trifluoromethyl-phenyl ring. Since the prior art does not disclose or suggest the -O-(CR¹R²)-(Alk¹)_n-C(O)-Y chain described in the present application in relation with selective androgen modulators, the provision of the compounds of the present application as further selective androgen modulators is regarded as not obvious and does involve an inventive step in the sense of Article 33(3) PCT.

3. Industrial Applicability

3.1 The subject-matter of claims 1 - 9 and 11 - 15 is industrial applicable.

3.2 For the assessment of the present claim 10 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not

recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.